Amendments to the Claims:

1. (Currently Amended) A method of ~~labeling~~ identifying a protein exposed on a luminal surface of a cell lining of a perfusible space *in situ* or *in vivo* comprising the following steps:

   (a) providing a cell membrane impermeable reagent comprising three domains

      (i) a first domain comprising a chemical moiety capable of covalently and non-specifically binding to the protein exposed on the luminal surface of a cell lining of a perfusible space *in situ* or *in vivo*,

      (ii) a second domain comprising a labeling domain, and

      (iii) a third domain situated between the first and second domains linking the first domain to the second domain by a cleavable chemical moiety, wherein the cleavable chemical moiety comprises a disulfide group, a periodate-cleavable glycol, a dithionite-cleavable diazobond, a hydroxylamine-cleavable ester, or a base-labile sulfone;

   (b) administering the membrane impermeable reagent into the perfusible space in an intact organ or an intact animal to react the cell membrane impermeable reagent with ~~the~~ proteins exposed on the luminal surface of the cell lining of the perfusible space to label the lumen-exposed protein; and

   (c) ~~cleaving the cleavable chemical moiety of the reagent that reacted with the lumen-exposed protein under a condition that does not denature the lumen-exposed protein~~ identify a lumen exposed protein under a condition that does not denature the protein.

2. (Previously Amended) The method of claim 1, wherein the reagent-reacted lumen-exposed protein is an organ-specific or a tissue-specific protein.

3. (Original) The method of claim 1, wherein the perfusible space is a lumen of a vascular vessel and the cell lining the space is an endothelial cell.

4. (Original) The method of claim 3, wherein the vascular vessel is an artery, an arteriole, a vein, or a capillary.

5. (Original) The method of claim l, wherein the perfusible space is a lumen of a cerebral spinal fluid (CSF) space.

6. (Original) The method of claim 1, wherein the perfusible space is a lumen of a lymphatic vessel and the cell lining the space is an endothelial cell.

7. (Original) The method of claim 1, wherein the perfusible space is a lumen of an endocrine or exocrine duct or pore.

8. (Original) The method of claim 1, wherein the cell lining the perfusible space is an epithelial cell.

9. (Original) The method of claim 1, wherein the organ is, or the tissue is derived from, a heart, a lung, a brain, a liver, a kidney, an endocrine gland, skin, a reproductive organ, a digestive tract organ, or an eye.

10. (Previously Presented) The method of claim 1, wherein the labeling domain of the reagent is selected from the group consisting of an enzyme, biotin, a colorimetric moiety, a fluorescent moiety, a luminescent moiety, a bioluminescent moiety, a radionucleotide and a paramagnetic element.

11-12. (Cancelled)

13. (Original) The method of claim 1, wherein the cleavable chemical moiety comprises a disulfide group.

14-15. (Cancelled)

16. (Original) The method of claim 1, wherein administering the cell membrane impermeable reagent into the perfusible space of the intact organ or tissue or the intact animal comprises administration of a buffered, aqueous solution comprising the cell membrane impermeable reagent.

17-18. (Cancelled)

19. (Currently Amended) A method of isolating a protein that is exposed on a luminal surface of a perfusible space comprising the following steps:

(a) providing a cell membrane impermeable reagent comprising three domains

(i) a first domain comprising a chemical moiety capable of covalently and non-specifically binding to a protein expressed on the luminal surface of a cell lining a perfusible space *in situ* or *in vivo*,

(ii) a second domain comprising a binding domain;

(iii) a third domain situated between the first and second domains linking the first domain to the second domain by a cleavable chemical moiety, wherein the cleavable chemical moiety comprises a disulfide group, a periodate-cleavable glycol, a dithionite-cleavable diazobond, a hydroxylamine-cleavable ester, or a base-labile sulfone;

(b) administering the cell membrane impermeable reagent into the perfusible space in an intact organ or an intact animal to react the cell membrane impermeable reagent with a protein expressed on the luminal surface of the cell lining of the perfusible space; and

~~(c) cleaving the cleavable chemical moiety of the reagent that reacted with the lumen-exposed protein under a condition that does not denature the lumen-exposed protein.~~

(dc) isolating the reagent-reacted lumen-exposed protein by contacting the reagent-reacted lumen-exposed protein with a ligand; and.

(d) identify a lumen exposed protein under a condition that does not denature the protein.

20. (Previously Presented) The method of claim 19, wherein the lumen-exposed protein is an organ-specific or a tissue-specific protein.

21. (Previously Presented) The method of claim 20, further comprising the step of comparing the reagent-reacted proteins from different organs or tissues to identify the organ-specific or tissue-specific protein, wherein the organ-specific or tissue-specific protein is exposed on the luminal surface of the perfusible space of only one of the compared organs or tissues.

22. (Original) The method of claim 19, wherein the perfusible space is a lumen of a vascular vessel and the cell lining the space is an endothelial cell.

23. (Original) The method of claim 22, wherein the vascular vessel is an artery, an arteriole, a vein, or a capillary.

24. (Original) The method of claim 19, wherein the perfusible space is a lumen of a cerebral spinal fluid (CSF) space.

25. (Original) The method of claim 19, wherein the perfusible space is a lumen of a lymphatic vessel and the cell lining the space is an endothelial cell.

26. (Original) The method of claim 19, wherein the perfusible space is a lumen of an endocrine or exocrine duct or pore.

27. (Previously Presented) The method of claim 19, wherein the cell lining of the perfusible space is an epithelial cell.

28. (Original) The method of claim 19, wherein the organ is, or the tissue is derived from, a heart, a lung, a brain, a liver, a kidney, an endocrine gland, skin, a reproductive organ, a digestive tract organ, or an eye.

29. (Previously Presented) The method of claim 19, wherein the ligand comprises of biotin.

30. (Previously Presented) The method of claim 19, wherein the ligand comprises a polypeptide, a nucleic acid, or a peptide nucleic acid.

31. (Withdrawn) The method of claim 30, wherein the polypeptide comprises a polyhistidine, a protein A domain, or a FLAG extension.

32. (Original) The method of claim 19, wherein the cleavable chemical moiety comprises a disulfide group.

33-35. (Cancelled)

36. (Original) The method of claim 19, wherein administering the cell membrane impermeable reagent into the perfusible space of the intact organ or tissue or the intact animal comprises administration of a buffered, aqueous solution comprising the cell membrane impermeable reagent.

37-38. (Cancelled)

39. (Original) The method of claim 19, wherein two separate cell membrane impermeable reagents are co-administered.

40. (Previously Presented) The method of claim 19, wherein the reagent-reacted protein is isolated by

(a) contacting a cell or a membrane isolate or a cell or a tissue homogenate or an extract derived from the reagent-reacted organ or animal with a ligand having affinity for the binding domain of the cell membrane impermeable reagent; and

(b) removing a non-bound protein from the ligand-bound proteins.

41. (Original) The method of claim 40, wherein the ligand is immobilized.

42. (Original) The method of claim 41, wherein the ligand is immobilized on a bead.

43. (Previously Presented) The method of claim 40, wherein the ligand is an avidin or a strepavidin molecule.

44. (Previously Presented) The method of claim 40, wherein the reagent-reacted protein is further isolated by removing substantially all of the non-bound protein from the ligand-bound proteins.

45. (Previously Presented) The method of claim 40, wherein the non-bound protein is removed by washing.

46. (Previously Presented) The method of claim 40, wherein the cleaving step does not dissociate the ligand from the binding domain after removing a non-bound protein.

47-48. (Cancelled)

49. (Previously Presented) The method of claim 46, wherein the ligand-bound lumen-exposed protein is further isolated by elution from the binding domain and the ligand.

50. (Cancelled)

51. (Currently Amended) A method of isolating an organ-specific or tissue-specific protein that is exposed on a luminal surface of an arteriole, a capillary or a vein comprising the following steps:

(a) providing a cell membrane impermeable reagent comprising three domains

(i) a first domain comprising an active moiety capable of covalently and non-specifically binding to a protein expressed on the luminal surface of a cell lining a perfusible space *in situ* or *in vivo*,

(ii) a second domain comprising a biotin binding domain, and

(iii) a third domain comprising a disulfide moiety situated between the first and second domains linking the first domain to the second domain; and

(b) administering the cell membrane impermeable reagent into a lumen of an artery, a arteriole, a capillary or a vein in an intact organ or an intact animal to react the cell membrane impermeable reagent with a protein expressed on the luminal surface; and

(cd) isolating the reagent-reacted protein by contacting the reagent-reacted protein with an immobilized avidin or streptavidin molecule; and

(de) ~~removing substantially all of the non-immobilized proteins~~ identify a lumen exposed protein under a condition that does not denature the protein.

~~(f) cleaving the cleavable chemical moiety of the reagent that reacted with the lumen exposed protein under a condition that does not denature the lumen-exposed protein.~~

52-55. (Cancelled)

56. (Previously Presented) The method of claim 10, wherein the enzyme is selected from the group consisting of horseradish peroxidase, alkaline phosphatase, β-galactosidase, and acetylcholinesterase.

57. (Previously Presented) The method of claim 10, wherein the bioluminescent moiety is selected from the group consisting of luciferase, luciferin, and aequorin.

58. (Previously Presented) The method of claim 10, wherein the radionucleotide is selected from the group consisting of H-3, S-35, I-125, I-131, P-32, Y-90, Re-188, At-211, and Bi-212.

59. (Previously Presented) The method of claim 10, wherein the paramagnetic moiety is selected from the group consisting of Cr, V, Mn, Fe, Co, Ni, Cu, La, Ce, Pr, Nd, Pm, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, and Lu.

60. (Previously Presented) The method of claim 10, wherein the fluorescent moiety is selected from the group consisting of umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride, and phycoerythrin.

61. (Previously Presented) The method of claim 51, further comprising the step of cleaving the cleavable chemical moiety of the cell membrane impermeable reagent under a condition that does not dissociate said immobilized avidin or streptavidin protein from said biotin binding domain.

62. (Previously Presented) The method of claim 51, further comprising the step of comparing the reagent-reacted proteins from different organs or tissues to identify the organ-specific or tissue-specific protein.

63. (Previously Presented) the method of claim 52 wherein the organ-specific or tissue-specific protein is detected in only one tissue.